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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,464	04/05/2005	Tara Nylese	10442-004	4794

29391 7590 06/17/2009

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EXAMINER	
DIRAMIO, JACQUELINE A	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
06/17/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,464	NYLESE, TARA	
	Examiner	Art Unit	
	JACQUELINE DIRAMIO	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10,11,15,16,18-21 and 25-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10,11,15,16,18-21 and 25-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Applicant's amendments to claims 1, 10, 19, 20, 25 and 26 are acknowledged.

2. Currently, claims 1, 10, 11, 15, 16, 18 – 21 and 25 – 29 are pending and under examination.

Withdrawn Objections and Rejections

3. The previous objections to claims 10 and 20 are withdrawn in view of Applicant's amendments filed April 2, 2009.

4. The previous rejection of claim 19 under 35 U.S.C. 112, second paragraph, is withdrawn in view of Applicant's amendments filed April 2, 2009.

5. All previous rejections of the claims under 35 U.S.C. 103(a) are withdrawn in view of Applicant's amendments and arguments filed April 2, 2009.

Response to Arguments

6. Applicant's arguments, see page 8, filed April 2, 2009, with respect to the rejection(s) of the claim(s) under 35 U.S.C. 103(a) as being unpatentable over Catt et al. (US 6,403,380) in view of Boehringer et al. (WO 98/39657) have been fully considered and are persuasive. In particular, Applicant's argument that neither Catt et al. nor Boehringer et al. teach the amendments to the independent claims, which require the monitoring of an "abnormal change" in a health condition, is found persuasive. Therefore, the rejections have been

withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Rutanen (US 2005/0136490).

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 10, 15, 19, 20 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10, lines 7, 9, 10, 12, 14, 15, 18, and 19, recite the term "the source," which lacks antecedent basis.

Claims 15 and 19 recite the term "the source," which lacks antecedent basis.

Claim 20, lines 5, 7, and 11, recite the term "the source," which lacks antecedent basis.

Claim 25, lines 6, 7, 8, 10, 12, 15, and 21, recite the term "the source," which lacks antecedent basis.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 1, 10, 11, 15, 16, 19 – 21, 25, 26, 28 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rutanen (US 2005/0136490) in view of Boehringer et al. (US WO 98/39657).

Rutanen teaches a method for monitoring whether an abnormal change occurs during a pregnancy (in a health condition) based on whether a change in a level of analyte concentration, particularly Insulin-like Growth Factor Binding Protein 1 (IGFBP-1), occurs in a source, comprising:

providing multiple analyte tests, wherein each test can comprise a nitrocellulose membrane strip (unitary test device) with an attached first antibody for binding to the analyte of interest and a labeled antibody for indicating the presence of the analyte in the source;

bringing a first sample from the source to conduct a first analyte test, wherein the first analyte test can comprise the contacting of the sample with the membrane strip (unitary test device), at a first time to induce, at the first time, there being a visually observable response on the membrane strip if the source contains at least a minimum of analyte concentration (i.e. IGFBP-1); and

subsequently bringing a second and subsequent sample from the same source (i.e. patient) to conduct a second analyte test, wherein the second analyte test can comprise the contacting of the sample with a second membrane strip at a second time, in order to determine whether a change in the pregnancy occurs based on whether an abnormal change in analyte level occurs by the second time, there again being a visually observable response on the second analyte test if the source contains at least a minimum level of analyte concentration, wherein determination of whether the pregnancy changes adversely can be based on capillary flow of each sample from a region on a membrane strip, and the response on each membrane strip is based on an amount of binding of an antigen and an antibody to form complexes (see paragraphs [0016], [0020], [0024]-[0029], [0032], [0034], [0039], [0041]-[0045], [0050], [0054], [0055], [0059], [0067]; Tables 2 and 3; and Example 3).

Rutanen discusses the use of several reagents to indicate different concentrations of analyte (i.e. IGFBP-1) in the sample (see paragraphs [0050] and [0067]). However, Rutanen fails to specifically teach that each of the membrane strips (unitary test devices) include a plurality of regions, each region responsive at a different sensitivity level to indicate the presence of the analyte in the source, wherein the response in one or more regions is determined based on capillary flow of said sample from a sample receiving region on each of the membrane strips to one or more of the plurality of regions on the same test device.

Boehringer et al. teach a device and method for determining analyte concentration in a test sample. The method comprises providing a lateral flow device comprising a sample receiving zone, and one or more serially oriented capture zones, wherein the one or more capture zones are responsive at a different sensitivity level to indicate the presence of the analyte in the

test sample. Sample is applied to the sample receiving zone and allowed to migrate by capillary action to each of the one or more capture zones. Each capture zone is capable of providing a visually observable response, based on specific binding, including antigen-antibody binding, wherein a pattern of visually observable responses is created out of the one of more capture zones, which can be correlated to the analyte concentration in the test sample, thereby allowing for visually quantifying the amount of analyte in the sample (see Figure 1; p4, lines 22-38; p5, lines 1-2; p6, lines 15-19; column 7, lines 13-32; p12, lines 1-38; p13, lines 1-38; p14, lines 1-29; p15, lines 3-32; and Tables 1-3 on p41).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the method of Rutanen a plurality of regions on each of the membrane strips (test devices), wherein each region is responsive at a different sensitivity level, as taught by Boehringer et al. because Boehringer et al. teach the benefit of providing a lateral flow device with a plurality of capture zones, wherein each capture zone is responsive at a different sensitivity level to an analyte present in a sample, in order to create a pattern of visually observable responses out of the one of more capture zones, which can be correlated to the analyte concentration in the test sample, thereby allowing for visually quantifying the amount of analyte in the sample.

With respect to Applicant's claim 10, Rutanen teaches a method for monitoring abnormal changes during a pregnancy (in a health condition), comprising:

providing first and second analyte tests, wherein the analyte test can comprise a nitrocellulose membrane strip (lateral flow test unit) of the type which includes a receiving zone

for fluid samples and which is responsive by binding an antigen and an antibody in order to identify the presence of analyte in the source;

providing a first sample from the source at a first time;

conducting a first analyte test on the first sample, which can comprise bringing the first sample into contact with the receiving zone of the membrane strip (first unit) to provide an indication as to whether analyte (i.e. IGFBP-1) is present in the first sample at at least a first sensitivity level;

providing a second sample from the source (i.e. patient) at a second time subsequent to providing the first sample to determine whether an adverse change, such as a preterm pregnancy, in the pregnancy occurs; and

conducting a second analyte test on the second sample, which can comprise bringing the sample into contact with the receiving zone of a second membrane strip (first unit) to provide an indication as to whether analyte (i.e. IGFBP-1) is present in the second sample at at least a first sensitivity level;

wherein an abnormal difference between visually observable responses induced during the first analyte test at the first time and induced in the second analyte test at the second time, each based on binding of an antigen and antibody, provides information about whether an adverse change in the pregnancy has occurred between the two times (see paragraphs [0016], [0020], [0024]-[0029], [0032], [0034], [0039], [0041]-[0045], [0050], [0054], [0055], [0059], [0067]; Tables 2 and 3; and Example 3).

However, as discussed above, Rutanen fails to teach that the first and second analyte tests comprise lateral flow devices each of the type which includes a receiving zone for fluid samples

separated from two or more regions, each region responsive to analyte migrating from the receiving zone by capillary flow into the region, the two or more regions on each test unit defining multiple measurably distinguishable sensitivity levels each distinguishable sensitivity level indicative of a different amount of analyte in the source, wherein the first and second test units include first and second regions of measurably distinguishable sensitivity levels that are responsive by binding antigen and antibody in order to identify presence of analyte in the source.

Again, as discussed above, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the method of Rutanen a plurality of regions on each of the analyte tests or membrane strips, wherein each region is responsive at a different sensitivity level, as taught by Boehringer et al. because Boehringer et al. teach the benefit of providing a lateral flow device with a plurality of capture zones, wherein each capture zone is responsive at a different sensitivity level to an analyte present in a sample based on antigen-antibody binding, in order to create a pattern of visually observable responses out of the one of more capture zones, which can be correlated to the analyte concentration in the test sample, thereby allowing for visually quantifying the amount of analyte in the sample.

With respect to Applicant's claim 11, Boehringer et al. teach that test unit can include a second capture line responsive to presence of the second level of analyte and the step of bringing the sample into contact with the test unit includes providing said second capture region an opportunity to indicate the presence of analyte in the sample at at least the second sensitivity level (see Figure 1; p4, lines 22-38; p5, lines 1-2; p6, lines 15-19; column 7, lines 13-32; p12, lines 1-38; p13, lines 1-38; p14, lines 1-29; p15, lines 3-32; and Tables 1-3 on p41).

With respect to Applicant's claims 15 and 16, Boehringer et al. teach that the test unit can include forming thereon at least three capture lines each responsive to the presence of the analyte in the source at a different of the multiple distinguishable sensitivity levels (see Figure 1; p4, lines 22-38; p5, lines 1-2; p6, lines 15-19; column 7, lines 13-32; p12, lines 1-38; p13, lines 1-38; p14, lines 1-29; p15, lines 3-32; and Tables 1-3 on p41).

With respect to Applicant's claim 19, Boehringer et al. teach that the step of defining the multiple measurably distinguishable sensitivity levels each indicative of a different amount of analyte in the sample is accomplished by forming at least the first and second capture lines (see Figure 1; p4, lines 22-38; p5, lines 1-2; p6, lines 15-19; column 7, lines 13-32; p12, lines 1-38; p13, lines 1-38; p14, lines 1-29; p15, lines 3-32; and Tables 1-3 on p41).

With respect to Applicant's claim 20, Rutanen teaches a method for determining whether an abnormal change is occurring during a pregnancy (in a health condition), comprising:

providing two or more analyte tests, wherein each analyte test can comprise a nitrocellulose membrane strip (test unit) to receive analyte by capillary flow from a receiving zone;

bringing a first sample from a source for conducting a first analyte test, which can comprise contacting the sample with a membrane strip (unit) to indicate whether the analyte (i.e. IGFBP-1) is present in the sample at at least one level; and

on an occasion subsequent to providing the first sample, determining whether an adverse change, such as a preterm pregnancy, occurs in the pregnancy by conducting a second analyte test, which can comprise the bringing of a sample from the source into contact with a second membrane strip to indicate whether analyte is present in the second sample at at least one level,

wherein abnormal differences in indications on different analyte tests provide evidence as to whether there has been an adverse change in the pregnancy (see paragraphs [0016], [0020], [0024]-[0029], [0032], [0034], [0039], [0041]-[0045], [0050], [0054], [0055], [0059], [0067]; Tables 2 and 3; and Example 3).

However, as discussed above, Rutanen fails to teach that the two or more test units include multiple regions positioned thereon to receive analyte by capillary flow from a receiving zone, each region in each unit responsive to the presence of analyte in the source at a sensitivity level measurably distinguishable from another region in the same test unit, wherein two or more regions on each unit are responsive components in a ligand recognition system to provide different indications of analyte level allowing comparison of responses among regions on different test units based on levels of association of a detector reagent with a capture reagent resulting from migration of analyte from an associated receiving zone to the regions by capillary flow.

Again, as discussed above, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the method of Rutanen a plurality of regions on each of the analyte tests or membrane strips, wherein each region is responsive at a different sensitivity level, as taught by Boehringer et al. because Boehringer et al. teach the benefit of providing a lateral flow device with a plurality of capture zones, wherein each capture zone is responsive at a different sensitivity level to an analyte present in a sample based on antigen-antibody binding, in order to create a pattern of visually observable responses out of the one of more capture zones, which can be correlated to the analyte concentration in the test sample, thereby allowing for visually quantifying the amount of analyte in the sample.

With respect to Applicant's claim 21, Boehringer et al. teach that the device is prepared by adhesively mounting the various zones and/or regions to a substrate (see p39, lines 8-37).

With respect to Applicant's claim 25, the limitations of this claim are discussed above with respect to Applicant's claim 20.

With respect to Applicant's claim 26, Rutanen teaches that the analyte test(s) is configured to indicate the health of a pregnancy, and wherein the second occasion is at least one day after the first occasion, the method indicating abnormal health of the pregnancy based on whether analyte concentration has increased between the first and second occasions (see paragraphs [0016], [0024], [0032], [0041]-[0045] and [0059]; and Tables 2 and 3).

With respect to Applicant's claims 28 and 29, Rutanen teaches that the first and second analyte tests, which can comprise nitrocellulose membranes (test units), are separate and apart from one another (see paragraphs [0041]-[0045], [0054] and [0055]; Tables 2 and 3; and Example 3).

9. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rutanen (US 2005/0136490) in view of Boehringer et al. (WO 98/39657), as applied to claims 10 and 16 above, and further in view of Cole (US 6,656,745).

The Rutanen and Boehringer et al. references, which were discussed in the 103(a) rejection above, fail to teach that each of the regions of the first test unit is responsive to substantially the same level of analyte as one of the regions of the second.

Cole teaches a device and method for multi-level, semi-quantitative immunodiffusion assay. The device utilizes a plurality of binding zones wherein the concentration of binding

agent immobilized determines a sensitivity of a given binding zone. Individual binding zones can be reactive for pre-determined levels of analyte in a sample, i.e. each binding zone has a specified concentration of binding reagent. Therefore, the binding zones allow for testing of an analyte over a broad range of concentration. The device normally involves a three-binding zone device or "tri-level test." The number of levels can be tailored in combination with the concentration of binding reagents to alter the sensitivity of the semiquantitative analysis depending on the particular application or desired precision. The device can detect for the presence or absence of the analyte, i.e. by determining trace levels of the analyte, as well as the semiquantitative amount of analyte present. Thus, the device is beneficial to screen for detection and progress of a particular medical condition, e.g. one threshold level can indicate that the condition is at a preliminary stage, whereas another threshold amount can indicate that the condition is in an advanced state. Such devices are beneficial for testing of analytes that occur in a range, such as prostate specific antigen (PSA) or pregnancy hormone (HCG), whose concentration range determines what, if any medical action is necessary (see column 5, lines 16-67; column 6, lines 7-48; and column 7, lines 16-50).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to create the regions of the first unit to be responsive to substantially the same level of analyte as only one of the regions of the second unit of Rutanen and Boehringer et al. in order to allow for testing of an analyte over a broad range of concentration as taught by Cole because Cole teaches the benefit of semiquantitative testing of analytes that occur in a range, such as prostate specific antigen (PSA) or pregnancy hormone (HCG), whose concentration range determines what, if any medical action is necessary.

10. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rutanen (US 2005/0136490) in view of Boehringer et al. (WO 98/39657), as applied to claim 25 above, and further in view of Dart et al. ("Rate of Change of Serial β-Human Chronionic Gonadotropin Values as a Predictor of Ectopic Pregnancy in Patients with Indeterminate Transvaginal Ultrasound Findings," *Annals of Emergency Medicine*, Vol. 34, No. 6 (1999) 703-710).

Rutanen and Boehringer et al. further fail to teach that the tests or devices are configured to indicate the presence of chorionic gonadotropin as the analyte, wherein the second occasion is at least 72 hours after the first occasion, and the method indicates whether the analyte concentration has doubled between the first and second occasions.

Dart et al. teach a study and method of detecting the rate of change of β-Human Chronionic Gonadotropin (hCG) in patents with symptoms suggesting ectopic pregnancy. The study and method determined that patients with a rate of increase or decrease of 2 consecutive β-hCG assays was useful in predicting the likelihood of ectopic pregnancy, particularly those patients with abnormal increasing β-hCG values (see p703 "Study objective," p707 "Discussion," and Table 2).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the method of Rutanen and Boehringer et al. the detection of the increase of the analyte hCG over a specific timeframe as taught by Dart et al. because Dart et al. teach the importance of determining the increase or decrease of hCG in a pregnant patient through assaying on more than one occasion the hCG value because this increase or decrease in hCG, particularly an abnormal increase, is useful in predicting the likelihood of ectopic pregnancy.

Conclusion

11. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JACQUELINE DIRAMIO whose telephone number is (571)272-8785. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jacqueline DiRamio/
Examiner, Art Unit 1641

/Bao-Thuy L. Nguyen/
Primary Examiner, Art Unit 1641
June 16, 2009